

**ABSTRACT**

The present invention relates to binding pockets of Skp1-Cdc53/Cullin-F-box protein (SCF) E3 ubiquitin ligases associated with substrate selection and/or orientation. In particular, the invention relates to a crystal comprising such binding pockets. The crystal may be useful for modeling and/or synthesizing mimetics of a binding pocket or ligands that associate with the binding pocket. Such mimetics or ligands may be capable of acting as modulators of the interactions of a SCF E3 ubiquitin ligase and its substrates, and they may be useful for treating, inhibiting, or preventing diseases modulated by such interactions. Methods are also provided for regulating a SCF E3 ubiquitin ligase comprising changing a binding pocket associated with substrate selection and/or orientation.